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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,716	04/05/2001	Michael Karpusas	A062 US	4368
7590		12/22/2005	EXAMINER	
Niki D. Cox		BORIN, MICHAEL L		
Biogen, Inc.		ART UNIT		
14 Cambridge Center		PAPER NUMBER		
Cambridge, MA 02142		1631		

DATE MAILED: 12/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/826,716

Applicant(s)

KARPUSAS ET AL.

Examiner

Michael Borin

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20 and 34-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20,34-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/27/2005 has been entered.

Status of the claims

Claims 20,34-37 are pending.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20,34-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.

A. The claims are amended to recite that the crystallographic coordinates of the I-domain are "substantially identical" to those listed in Table II of specification. The term "substantially identical" is vague and indefinite and is not explained in the specification. Consequently, it is not clear which crystals are encompassed by the scope of the instant claims.

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B. Claim 20, step c): It is not clear whether the step c) is a separate step, or a “wherein” proviso, similar to the proviso of claim 34.

C. It is not clear whether the evaluation step of claim 20 (step b), and “competition assay” step in claim 34 (step d) are *in vitro* or *in silico* steps. Examiner assumes the former, but applicant is invited to clarify.

D. Claim 34: With regard to the term “composition” it is not clear whether the term reflects a singular “chemical moiety” (i.e., as in claim 20), or a composition of components – in the latter case, the scope of the composition is unclear.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 34-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection. Claims 20, 34-37 introduce NEW MATTER as they use are directed, in part, to “complex comprising an I domain of the α_1 chain $\alpha_1 \beta_1$ integrin”. The disclosure of specification is limited to crystals (and use thereof) of fragment 143-340 of α_1 chain of $\alpha_1 \beta_1$ integrin, i.e., of I-domain of α_1 chain. See specification, p. 3-4,

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and Table 2 (p. 25+). The new claim language "complex comprising $\alpha_1 \beta_1$ integrin α_1 -I domain" (claim 20, line 3) and subsequent language " $\alpha_1 \beta_1$ integrin α_1 -I domain" (claim 20, lines 4,5,7,10,11; claims 34-37), which is clearly different from the terms used in the specification, is understood as a complex of the I domain with $\alpha_1 \beta_1$ integrin. There is no disclosure of a crystal of any "complex comprising an I domain of the α_1 chain $\alpha_1 \beta_1$ integrin", nor there is any disclosure of using of crystallographic coordinates of any such complex.

Claims 20, 34-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection. Claims 20, 34-37 introduce NEW MATTER as they use are directed to use of crystals which have coordinates which are "substantially identical" to those listed in Table II. There is no disclosure of use of any crystals, other than the crystal of the I domain with coordinates disclosed in the Table II itself, and of any structural coordinates having coordinates different from, albeit substantially identical to, the coordinates disclosed in Table II.

Claim Rejections - 35 USC § 103

Claims 20,34,35 are rejected under 35 U.S.C. 103(a) as being obvious over Lee et al in view of Qu et al.

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The instant claims are directed to method of evaluating ability of a chemical entity to associate with an I-domain of the $\alpha_1 \beta_1$ integrin by using crystallographic coordinates of the I-domain to obtain data related to the association, and evaluating the degree of the association in a competition assay. The crystallographic coordinates of the I-domain are "substantially identical" to those listed in Table II of specification

Lee describes I domain crystals obtained from CD11b/CD18 obtained using an alkaline solvent) comprising PEG with subsequent freezing of the crystal before the data collection. (see p. 1139, section Materials and Methods, first two paragraphs). Lee describes structural characteristics of the I domain crystal and its association with metal cations (see abstract).

The I domain crystals described in Lee are obtained from CD11b/CD18 which, unlike the $\alpha_1 \beta_1$ integrin addressed in the instant claim is β_2 integrin. Thus, Lee does not teach use of crystallographic coordinates of the I-domain of the $\alpha_1 \beta_1$ integrin. However, Lee et al teaches that integrins are the $\alpha \beta$ heterodimers with a generally conserved structure (p. 1338, right column, last full paragraph) and that the I domain is a common motif in integrins containing α subunit. See p. 1133, last full paragraph, p. 1134. Thus, it would be obvious to an artisan that crystallographic coordinates of I-domain obtained from one integrin can be used to evaluate ability of a chemical entity to associate with an I-domain of another integrin, such as I-domain from $\alpha_1 \beta_1$ integrin. As to the claim limitation requesting that the crystallographic coordinates of the I-domain are "substantially identical" to those listed in Table II of specification, as Lee teaches

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that I domains in integrins are similar, their coordinates would be expected to be “substantially identical” in the absence of evidence to the contrary.

Further, Lee reference does not specifically address use of information obtained from fitting crystallographic information of I-domain and a query chemical entity in a subsequent *in vitro* evaluation of the degree of such association using a competition assay. The study described in Lee is a purely *in silico* structural study. However, the need to verify results of an *in silico* structural study with a subsequent *in vitro* testing is well known in the art and will be obvious to an artisan as a result of a routine optimization. Indeed, Lee, having discussed *in silico* observations of interactions of cations with the I domain, suggest the need for further *in vitro* biochemical testing. p. 1338, left column, end of the last full paragraph.

Further, with respect to of evaluating abilities to associate with the I domain for chemical entities other than metal cations addressed in Lee, Ou et al, conducting similar studies in crystal of I domain, teaches Mn-bound form of the I domain is the active configuration essential for ligand binding (see h p. 10279, right column, last paragraph, and p. 10277, Introduction section) and that that I-domain contains binding sites for such physiological ligands as ICAM-1 and ICAM-3 (p. 10279, left column, bottom). Although neither Lee nor Qu references perform direct “fitting operations” with ligands other than Mn²⁺, it would be *prima facie* obvious to one skilled in the art at the time the invention was made to employ the structural coordinates of crystal of I-domain obtained by Lee or Qu to identify interaction of $\alpha 1 \beta 1$ integrin with its ligands, such as ICAMs.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.
Primary Examiner
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